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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,395	06/07/2000	Avi J. Ashkenazi	P1759R1	9150

7590 05/20/2003

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EXAMINER

NICKOL, GARY B

ART UNIT PAPER NUMBER

1642

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicant(s)

09/589,395

Applicant(s)

ASHKENAZI ET AL.

Examiner

Gary B. Nickol Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1)  Responsive to communication(s) filed on 06 March 2003.
- 2a)  This action is **FINAL**.                      2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4)  Claim(s) 6-13 and 19-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) 6-13 and 19-43 is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a)  All    b)  Some    \* c)  None of:
1.  Certified copies of the priority documents have been received.
  2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a)  The translation of the foreign language provisional application has been received.
- 15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4)  Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5)  Notice of Informal Patent Application (PTO-152)
- 6)  Other:

***Response to Arguments***

The Response filed March 6, 2003 (Paper No. 19) in response to the Notice of Non-responsiveness mailed February 14, 2003 has been considered. Applicants have reiterated their remarks of Paper No. 16 (filed November 20, 2002) stating that the October 25, 2002 Response was indeed compliant because "no changes or amendments to the pending claims were requested by Applicants". Upon reconsideration and review, this argument is persuasive. The Office apologizes for the inconveniences.

Claims 6-13 and 19-43 are pending and are currently under consideration.

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**Rejections Maintained:**

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Claims 6-13, and 19-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ashkenazi *et al.* (US 6,252,050, June 12, 1998) or Ashkenazi *et al.* (WO 98/51793, November 1998, IDS # 14) in view of Keane *et al.* (Cancer Research, Vol. 59, pages 734-741, February 1999) and Rougier *et al.* (Semin.Oncol, 1996, Vol. 23, Abstract only) for the reasons of record in Paper No. 12, pages 3-5.

Applicants argue (Paper No. 19, page 2) that the art cited by the Examiner does not teach or suggest any reasonable expectation those skilled in the art that such agents could be combined

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to achieve a synergistic effect in inducing apoptosis in mammalian cancer cells. Applicants appear to base this position on the teachings of Rougier *et al* wherein the Office had reported that Rougier *et al.* taught that CPT-11 appears to have activity *similar* to that of 5-fluorouracil (5-FU) in first-line treatment. In contrast, Applicants argue that the abstract does not suggest similarity to 5-FU because the subsequent text in the abstract stated that CPT-11 remains active after failure of 5-FU therapy. Applicants further point to the specification wherein the CPT-11 product, (Camptostar®), can be used for the treatment of patients whose disease has recurred or progressed following 5-Fu based therapy. These arguments have been considered but are not found persuasive. Applicants appear to be basing their conclusions that CPT-11 and 5-FU are not “one and the same” because of any perceived failure of 5-FU in patients. However, the fact that CPT-11 can provide some sort of benefit to cancer patients following tumor recurrence or progression in patients that had received 5-FU-administered therapy does not establish that one drug is more efficacious than the other or that the two drugs do not have similar activity.

Recurrence and or progression of cancer in patients following chemotherapy is a well-established phenomenon due, in part, to genetic events invoking tumor cell resistance. And, oncologists are known to switch chemotherapeutics when one drug has failed to provoke an anti-tumor response or when resistance has been occurred. What is established is that both CPT-11 and 5-FU appear to have “similar activity” which provides a nexus to the data observed by Keane *et al.* wherein incubation of cells lines with the chemotherapeutic drugs doxorubicin or 5-fluoruracil significantly augmented TRAIL-induced apoptosis. With regards to Keane *et al.*, however, Applicants argue that Keane *et al.* teaches away from any expectation that a combination of chemotherapy, such as CPT-11, and TRAIL (Apo-2 ligand) would exert synergistic action

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because the abstract teaches the exact opposite. This argument has been considered but is not found persuasive because the abstract clearly teaches, "the toxicity of the combination of TRAIL and doxorubicin or 5-FU was synergistic compared with either agent alone" which does not present itself as a teaching away from, in particular, 5-FU chemotherapeutic augmentation of TRAIL-induced apoptosis. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

No claim is allowed.

*Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol Ph.D.  
Examiner  
Art Unit 1642

GBN  
May 9, 2003

  
ANTHONY C. CAPUTA  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600